

THORNDIKE MEMORIAL LABORATORY
SECOND AND FOURTH MEDICAL SERVICES
HARVARD MEDICAL UNIT
BOSTON CITY HOSPITAL

Research Grant NSG 595
National Aeronautics and Space Administration

A Study of Physiological Mechanisms and Inter-Relations
between Systemic and Regional Blood Volume, Blood
Flow and Electrolyte Balance

Walter H. Abelman, M. D.
Laurence E. Earley, M. D.

Interim Progress Report
December 31, 1965

FACILITY FORM 602

N 66-17072	
(ACCESSION NUMBER)	(THRU)
10	1
(PAGES)	(CODE)
CR 70316	04
(NASA CR OR TMX OR AD NUMBER)	(CATEGORY)

GPO PRICE \$ _____
CFSTI PRICE(S) \$ _____
Hard copy (HC) 1.00
Microfiche (MF) .50

11 653 July 85

(1) Renal Hemodynamics, Sodium Excretion, and Extracellular Volume

Previously described studies in the dog investigating the physiologic role of renal hemodynamics in the regulation of sodium excretion and the extracellular fluid volume have been continued. Some phases of this project have been completed, and reprints of published work are appended.

It has been demonstrated that extensive expansion of the extracellular fluid volume results in increased renal blood flow and probably a redistribution of blood flow within the kidney. Furthermore, these changes in renal blood flow correlate well with increased sodium excretion and decreased tubular reabsorption of sodium. These observations were extended to demonstrate that unilaterally increased renal blood flow (produced by renal arterial infusions of vasodilators) results in increased sodium excretion and decreased tubular reabsorption of sodium in the absence of extracellular fluid volume expansion. The combination of renal vasodilatation and increased arterial perfusion pressure produced by infusions of angiotensin or norepinephrine results in an even greater increased excretion of sodium and decreased reabsorption of sodium. These changes in sodium excretion and reabsorption occur independent of both changes in glomerular filtration rate and the renal tubular effects of adrenal salt-retaining steroids. On the basis of these observations it has been concluded tentatively that renal vascular resistance and arterial perfusion pressure may be important factors in the regulation of sodium excretion and the

extracellular fluid volume.

Studies in progress have been designed to assess the role of these hemodynamic factors (renal vascular resistance and perfusion pressure) in states of sodium retention. These projects are being carried out in both the dog with experimental sodium retention (supra-hepatic inferior vena caval constriction) and in man with salt and water retention secondary to liver disease. It has already been observed in the dog that such retention of sodium may be reversed by increasing arterial pressure and renal blood flow.

(2) The Effect of Mitral Stenosis and Atrial Fibrillation Upon the Excretion of a Sodium Load, with Observations on the Effect of Cardioversion

In order to explore the possible role of obstruction at the mitral valve and of atrial distention and atrial fibrillation upon the retention of sodium and water, six patients with mitral stenosis of varying severity, in balance on a 50 mEq. sodium diet were given an infusion of 308 mEq. of sodium in 2 liters of water over two hours. Whereas in normal subjects such a load was completely excreted in three days, the patients with mitral stenosis and atrial fibrillation excreted only an average of 47 per cent of the load in the same period of time. After electrical conversion to normal sinus rhythm in four of these patients, the excretion of the same sodium load uniformly increased to an average of 72 per cent after three days.

Surgical repair of mitral stenosis in one patient also was followed by increased excretion of the sodium load, notwithstanding persistence of atrial fibrillation. There was no relationship between sodium excretion and severity of the stenosis, left atrial pressure, cardiac output, heart rate, digitalis status, systemic pressure or clinical classification.

It is concluded that in patients with mitral stenosis and atrial fibrillation, excretion of the sodium load may be delayed and incomplete. Conversion to normal sinus rhythm by electrical counter-shock consistently increased the rate and completeness of the excretion of the sodium load. It appears that obstruction at the mitral valve and atrial fibrillation are factors that independently enhance sodium retention in the cardiac patient.

These studies are now being extended to patients with large left atria without obstruction at the mitral valve, and to patients with atrial fibrillation without obstruction at the mitral valve.

(3) The Effect of Abnormal Circulatory States Upon the Response of Heart Rate and Blood Pressure to Upright Tilt

The responses of heart rate and blood pressure to a 70° upright tilt for 30 minutes were studied in eight normal subjects, in thirty patients with heart disease, in four patients convalescing from pneumonia, and in three normal subjects after volume depletion.

While the eight normal subjects responded normally to vertical

tilt, increasing heart rate and narrowing pulse pressure, twelve of seventeen patients with left ventricular failure associated with hypertensive heart disease, primary myocardial disease, aortic valvular disease or mitral regurgitation showed an abnormal response, consisting of little or no increase in heart rate and no change or an increase in pulse pressure. Thirteen patients with rheumatic mitral stenosis studied on 21 occasions showed eleven normal responses, nine "heart failure responses", and one response suggesting autonomic insufficiency. Of the nine "heart failure responses", seven were associated with mild mitral stenosis and normal sinus rhythm. Four patients convalescing from pneumonia, studied in similar fashion, were unable to maintain their blood pressure, notwithstanding a significant increase of the heart rate in three. These patients all had small hearts, normal central venous pressures, and normal or low cardiac output instead of the expected hyperdynamic response to pneumonia. Central blood volume was diminished.

Three normal subjects, volume depleted by acute intravenous administration of ethacrynic acid, showed postural hypotension and marked tachycardia. Similar volume depletion in a patient with decompensated heart disease, did not result in postural hypotension.

The data suggest that in the presence of an enlarged left atrium, blood pressure may be maintained without tachycardia in the face of an upright tilt. On the other hand, in subjects without heart disease

a decrease in central blood volume tends to result in tachycardia and postural hypotension after upright tilt. Thus central blood volume may, in part, determine the response to tilting.

PUBLICATIONS

- (1) Earley, L. E. and Friedler, R. M.: Changes in renal blood flow and possibly the intrarenal distribution of blood during the natriuresis accompanying saline loading in the dog. J. Clin. Invest. 44: 929, 1965.
- (2) Earley, L. E. and Friedler, R. M.: Studies on the mechanism of natriuresis accompanying increased renal blood flow and its role in the renal response to extracellular volume expansion. J. Clin. Invest. 44: 1857, 1965.
- (3) Akbarian, M. and Abelmann, W. H.: Observations on the hypodynamic circulatory state in patients with acute pneumonia. Clin. Res. 13: 345, 1965 (Abstract).
- (4) Friedler, R. M. and Earley, L. E.: Combined effects of renal vasodilatation and vasopressors on renal hemodynamics and sodium excretion. Clin. Res. 13: 554, 1965 (Abstract).
- (5) Earley, L. E. and Friedler, R. M.: The effects of combined renal vasodilatation and pressor agents on renal hemodynamics and the tubular reabsorption of sodium. J. Clin. Invest. (in press).

Traveler No. 80-57, Contract No. NaG-595/22-07-019, has been reviewed by the Space Medicine Branch, NMC, and the resulting comments are presented in the following text.

The report is rather superficial and consists mainly of broad statements summarizing the general study plans and very general conclusions based upon the current data acquisition and analysis. However, the report alludes to appended reprints of published work, which were not available for review. It is assumed that these reports are more informative in their coverage which would allow comments pertinent to the validity of the research.

The research which is being conducted under this grant is basic. The information reported is applicable to the entirety of medical sciences. Generally speaking, studies of this nature are supported by National Institutes of Health grants.

The research work is consistent with the guideline of the original proposal and the progress of the work is highly satisfactory.

N 66-17 072